IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of Maria Laura Gennaro	)	
	)	Confirmation No.: 7070
Application No.: 10/009,383	)	
	)	Art Unit: 1645
Filed: March 4, 2002	)	
	)	Examiner: Rodney P. Swartz
Title: PROTEINS EXPRESSED BY MYCOBACTERIUM TUBERCULOSIS AND NOT BCG AND THEIR USE AS DIAGNOSTIC REAGENTS AND VACCINES	)	

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
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Sir:

Appellant submits this brief in accordance with the provisions of 37 C.F.R. §41.37 in response to the Final Office Action mailed September 16, 2009 (the "Final Office Action") and subsequent Advisory Action mailed February 4, 2009 (the "Advisory Action"). Appellant's Notice of Appeal was filed on March 16, 2009. This Appeal Brief is therefore timely filed.

I. REAL PARTY IN INTEREST

The real party in interest is the University of Medicine and Dentistry of New Jersey by virtue of an assignment executed by the inventor (Appellant) to Public Health Research Institute of the City of New York, Inc. on December 20, 2001 (recorded at Reel/Frame 018053/0867 on September 4, 2006), and an assignment executed by Public Health Research Institute of the City

of New York, Inc. to the University of Medicine and Dentistry of New Jersey on December 15, 2006 (recorded at Reel/Frame 018668/0554).

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF CLAIMS

In the application under appeal, claims 3-7, 9 and 10 (the "Pending Claims") are pending. Claims 1-2, 8, and 11-54 were previously cancelled. The Pending Claims stand rejected under 35 USC §103(a) as being unpatentable over WO98/16645, 23 April 1998 (hereinafter "Reed et al."). The 35 USC §103(a) rejection of the Pending Claims over Reed et al. are appealed.

IV. STATUS OF AMENDMENTS

In Appellant's response to Final Office Action dated December 16, 2008, Appellant amended claims 3, 4, and 7. The Examiner acknowledged these amendments in the Advisory Action. Therefore, all amendments prior to the close of prosecution on the merits have been entered. A current listing of the Pending Claims is submitted herewith in Section VIII.

V. SUMMARY OF CLAIMED SUBJECT MATTER

References herein to the present application are to the application as published (WO00/66157).

Independent claim 3 recites a vector comprising "a DNA sequence encoding a full length MTBN4 polypeptide, wherein the polypeptide is not encoded by the genome of the Bacille

Calmette Guerin (BCG) strain of *Mycobacterium bovis*." The DNA sequence encoding a full length MTBN4 polypeptide is described in the specification at least at page 2, line 15 and Figure 1.

The vector further comprises "at least one additional DNA sequence encoding a polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*." Such at least one additional DNA sequence is described in the specification at least at page 2, line 15, page 3, lines 1-5, and Figure 1.

Each DNA sequence of the recited vector is "operationally linked to a regulatory sequence allowing expression of the polypeptide encoded by each DNA sequence in a cell." This limitation is described in the specification at least at page 3, lines 6-7.

Independent claim 4 recites a vector comprising "a DNA sequence encoding a segment of a full length MTBN4 polypeptide, wherein said segment retains an antigenic property of the polypeptide and wherein the segment is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*." The DNA sequence encoding a segment of a full length MTBN4 polypeptide is described in the specification at least at page 2, lines 20-21 and Figure 1.

The vector further comprises "at least one additional DNA sequence encoding a segment of a full length polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*." Such at least one additional DNA sequence is described in the specification at least at page 2, line 15, page 3, lines 1-5, and Figure 1.

Each DNA sequence of the recited vector is "operationally linked to a regulatory sequence allowing expression of the segment encoded by each DNA sequence in a cell." This limitation is described in the specification at least at page 3, lines 6-7.

Independent claim 7 recites a composition comprising "a vector and a pharmaceutically acceptable diluent or filler, wherein the vector comprises a DNA sequence encoding a full length MTBN4 polypeptide and wherein the polypeptide is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis* and at least one additional DNA sequence encoding a polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*." The composition is described in the specification at least at page 2, line 11 through page 3, line 14, and Figure 1.

Independent claim 9 recites a composition comprising "at least two DNA sequences, each encoding a polypeptide of the *Mycobacterium tuberculosis* complex that is not a polypeptide encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, and each being operationally linked to a regulatory sequence which allows expression of said polypeptide in a cell of a vertebrate, wherein at least one of said DNA sequences encodes a full length MTBN4 polypeptide." The composition is described in the specification at least at page 2, line 11 through page 3, line 14, and Figure 1.

Independent claim 10 recites a composition comprising "at least two DNA sequences, each encoding a polypeptide of the *Mycobacterium tuberculosis* complex that is not a polypeptide encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, and each being operationally linked to a regulatory sequence which allows expression of said polypeptide in a cell of a vertebrate, wherein at least one of said DNA

sequences encodes a segment of a full length MTBN4 polypeptide." The composition is described in the specification at least at page 2, line 11 through page 3, line 14, and Figure 1.

References in this brief to supporting portions of the specification and drawings are given to provide exemplary embodiments, not to provide limitations to the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellant respectfully requests that the Board of Patent Appeals and Interferences review the following ground of rejection on appeal:

1. Whether the Pending Claims, i.e. claims 3-7, 9 and 10, are patentable under 35 USC §103(a) over Reed et al.

VII. ARGUMENT

Appellant respectfully submits that the Pending Claims are patentable over the prior art of record.

The Pending Claims are patentable over Reed et al.

The Pending Claims are rejected under 35 USC §103(a) over Reed et al. Appellant respectfully disagrees.

Appellant asserts that the Pending Claims are patentable over Reed et al. because Appellant contends that Reed et al. does not teach, suggest, or make obvious what is claimed by the Pending Claims of the present application.

In the Final Office Action, the Examiner contended that:

> Reed et al. do teach the claimed sequence of MTBN4, SEQ ID NO:110, and an isolated DNA comprising the DNA which encodes SEQ ID NO:110. In addition, Reed et al. do teach vectors and host cells comprising DNA. Thus, it would have been obvious to utilize the specific DNA encoding SEQ ID NO:110 for production of vectors and host cells.

The Examiner further contended in the Advisory Action that:

> [T]he teachings of Reed et al. would have suggested one of ordinary skill in the art to place the sequence into a vector, transform a host cell with that vector, and to admix said vector with a pharmaceutically acceptable diluent or filler as taught by Reed et al for the other DNA sequences in the document.

Appellant respectfully disagrees with these positions for the reasons set forth below.

1. Reed et al. does not teach or fairly suggest the selection of a DNA sequence encoding MTBN4 for combination with at least one additional DNA sequence encoding a polypeptide that is encoded by *M. tuberculosis* but that is not encoded by the genome of the BCG strain of *M. bovis* to yield the vectors, cells, and compositions of the Pending Claims.

Appellant submits that, in view of Reed et al., one of skill in the art would not have been motivated to create a vector, cell, or composition, comprising a DNA molecule or sequence encoding MTBN4 polypeptide and at least one additional DNA sequence encoding a polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, as recited in claims 3-7; or a composition comprising at least two DNA sequences, each encoding a polypeptide of the *Mycobacterium tuberculosis* complex that is not a polypeptide encoded by the genome of the BCG strain of *Mycobacterium bovis*, as recited in claims 9-10.

Appellant submits that, as acknowledged by the Examiner, Reed et al. do not teach vectors or host cells which incorporate SEQ ID NO:110, which is analogous to MTBN4 of the instant application. Appellant further submits that Reed et al. do not teach or suggest vectors or host cells which incorporate SEQ ID NO:110 in combination with at least one additional DNA sequence encoding a polypeptide which is encoded by *M. tuberculosis* but is not encoded by the genome of the BCG strain of *M. bovis*. The instant application teaches that MTBN4 is not encoded by BCG. The instant application also teaches the selection of at least one additional DNA sequence that, like MTBN4 is encoded by *M. tuberculosis* but is not encoded by BCG. Reed et al., on the other hand, does not teach whether any of the sequences disclosed therein are encoded by the BCG strain of *M. bovis*, and therefore provides no basis or guidance for selecting the at least one additional DNA sequence of the Pending Claims. Appellant respectfully reminds the Examiner that in order to avoid impermissible hindsight bias, "knowledge of applicant's disclosure must be put aside in reaching this [obviousness] determination, yet kept in mind in order to determine the 'differences,' conduct the search and evaluate the 'subject matter as a whole' of the invention. MPEP §2142. Reed et al. does not teach whether the sequences

disclosed therein are encoded by the BCG strain of *M. bovis* and therefore does not provide any motivation to create the vectors, cells, and compositions of the Pending Claims.

In further support of this position, Appellant respectfully directs the Examiner to Reed et al. at page 21, lines 24-27, which recites "[i]n embodiments in which more than one polypeptide is employed, the polypeptides used are preferably complementary (i.e., one component polypeptide will tend to detect infection in samples where the infection would not be detected by another component polypeptide)." According to the foregoing, the individual polypeptides combined in Reed et al. should have different characteristics in order to be complementary to each other. However, the polypeptides utilized in the combination of the present claims share similar characteristics, i.e. each polypeptide is encoded by *M. tuberculosis* but is not encoded by the genome of the BCG strain of *M. bovis*. Therefore, in view of the teachings of Reed et al., Appellant submits that one of skill in the art would not be motivated to create a vector, cell, or composition, comprising a DNA molecule or sequence encoding MTBN4 polypeptide and at least one additional DNA sequence encoding a polypeptide which is encoded by *M. tuberculosis* but is not encoded by the genome of the BCG strain of *M. bovis*, as recited in claims 3-7; or a composition comprising at least two DNA sequences, each encoding a polypeptide of the *M. tuberculosis* complex that is not a polypeptide encoded by the genome of the BCG strain of *M. bovis*, as recited in claims 9 and 10 of the present application.

In the Advisory Action, the Examiner stated that the above arguments had been considered, but were not found persuasive. However the Examiner's only stated basis for finding the above arguments unpersuasive was that "[t]he cited instance in Reed et al. is merely a 'preferred' embodiment and does not exclude other embodiments." Further, the Examiner's concluding sentence as to what "Reed et al would have suggested" to one of ordinary skill in the

art fails to even state that, in view of Reed et al., one of ordinary skill in the art would be motivated to create the vectors, cells, and compositions of the Pending Claims by: (i) selecting SEQ ID NO:110 from the 209 sequences disclosed by Reed et al; (ii) choosing to combine SEQ ID NO:110 with the DNA sequence of a second polypeptide; and (iii) further choosing that second DNA sequence on the basis of two similarities with SEQ ID NO:110, i.e. (1) it is encoded by *M. tuberculosis* and (2) it is not encoded by the genome of the BCG strain of *M. bovis*. Indeed, as discussed above, the prior art would actually motivate one skilled in the art to choose the second DNA sequence based on its differences with, not similarities to, SEQ ID NO:110. "Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Ex Parte Pekka J. Soininen and Sven Lindfors*, 2009 WL 492118 (Bd.Pat.App. & Interf.) (February 25, 2009). Appellant respectfully submits that the Examiner has not provided articulated reasoning as to why one of skill in the art would be motivated by Reed et al. to combine SEQ ID NO:110 with the DNA sequence of another polypeptide that is (1) encoded by *M. tuberculosis* and (2) not encoded by the BCG strain of *M. bovis*.

Even if, as the Examiner alleges, "Reed et al. would have suggested one of ordinary skill in the art to place the sequence into a vector, transform a host cell with that vector, and to admix said vector with a pharmaceutically acceptable diluent as taught by Reed et al for the other DNA sequences in the document," Appellant respectfully submits that Reed et al. simply does not provide the additional motivation to suggest that one of ordinary skill in the art both (i) further combine the SEQ ID NO:110 with the DNA sequence of another polypeptide and (ii) select the DNA sequence of the other polypeptide based on at least two factors, e.g. (a) whether it is

encoded by *M. tuberculosis* and (b) whether it is encoded by the genome of the BCG strain of *M. bovis*.

Appellant reiterates the previous argument that the instant claims call for a combination of polypeptides that share characteristics, e.g. both polypeptides are encoded by *M. tuberculosis* and neither polypeptide is encoded by the genome of the BCG strain of *M. bovis*. While Reed et al. does make a general reference to using the polypeptides in combination with each other, it does nothing to teach or suggest that one of ordinary skill in the art employ the particular combinations of the present invention, i.e. combining a sequence encoding MTBN4 with the sequence of another polypeptide that is encoded by *M. tuberculosis* but not the BCG strain of *M. bovis*. Indeed, Reed et al. does not even indicate which of the polypeptides disclosed therein are encoded by the BCG strain of *M. bovis* and which are not. Even if one skilled in the art wished to create the vectors, cells, and compositions of the Pending Claims, he would not be able to do so based on the teachings of Reed et al. The instant application recognizes that proteins encoded by ORFs present in the genome of *M. tuberculosis* but absent from the genome of BCG represent reagents that are useful in distinguishing between individuals who have been exposed to *M. tuberbculosis* and individuals who have been vaccinated with BCG. Reed et al., on the other hand, makes no such distinction and offers no guidance on how one of skill in the art could create the vectors, cells, and compositions of the Pending Claims, which can then be used to distinguish between these two classes of individuals. To import the novel insights of the instant application into the teachings of Reed et al. would constitute impermissible hindsight bias.

Even assuming, *arguendo*, that one of skill in the art were motivated to combine the DNA sequence of SEQ ID NO:110 of Reed et al. with another DNA sequence encoding a polypeptide with similar characteristics to that sequence, one of skill in the art would actually be

motivated by Reed et al. to choose a sequence that was encoded by *M. bovis*. On page 38, line 27, Reed et al. discloses that SEQ ID NO:110 "may be the homologue of Tb38-1." At line 18 of page 38, Reed et al. also discloses that "Tb38-1 was found to be located 34 base pairs upstream of the open reading frame for the antigen ESAT-6 previously identified in *M. bovis* . . . and *M. tuberculosis*." Because SEQ ID NO:110 is disclosed as a possible homologue of Tb38-1, and because Tb38-1 is taught by Reed et al as being located only 34 base pairs upstream from the open reading frame for an antigen identified as being encoded by *M. bovis*, one of skill in the art would be likely to conclude, based on the teachings of Reed et al., that SEQ ID NO:110 is also encoded by *M. bovis* and would likewise be likely to conclude that SEQ ID NO:110 is encoded by the genome of the BCG strain of *M. bovis*. Therefore, if one skilled in the art were motivated to combine SEQ ID NO:110 of Reed et al. with another DNA sequence encoding a polypeptide with similar characteristics to the polypeptide encoded by SEQ ID NO:110, Reed et al. would lead one of skill in the art to choose a polypeptide that is encoded by both *M. bovis* and *M. tuberculosis* because Reed et al. implies a likelihood that the homologue of SEQ ID NO:110 is found in both *M. bovis* and *M. tuberculosis*.

Reed et al. does not teach or suggest that one skilled in the art should: (i) select SEQ ID NO:110 from the 209 sequences disclosed by Reed et al; (ii) choose to combine SEQ ID NO:110 with the DNA sequence of a second polypeptide; and (iii) further choose that second DNA sequence on the basis of two similarities with SEQ ID NO:110, i.e. (1) it is encoded by *M. tuberculosis* and (2) it is not encoded by the genome of the BCG strain of *M. bovis*. Reed et al. also does not make any indication as to which of the polypeptides disclosed therein are encoded by the BCG strain of *M. bovis* and which polypeptides are not. These absences, taken together

with Reed et al.'s single reference to SEQ ID NO:110, compels the conclusion that Reed et al. does not teach or fairly suggest the vectors, cells, and compositions of the Pending Claims.

2. The DNA sequence combinations of the Pending Claims yield an additional advantage over the polypeptide combinations contemplated by Reed et al.

Appellant further respectfully submits that the DNA sequence combinations covered by the Pending Claims yield an additional advantage over the polypeptide combinations contemplated by Reed et al. The combinations of the Pending Claims capitalize on and exploit the fact that the *M. tuberculosis* polypeptides of the Pending Claims are not encoded by the BCG strain of *M. bovis*. The vectors, cells, and compositions of the Pending Claims that incorporate these combinations are thus able to distinguish between individuals that have been infected with tuberculosis and individuals that have been vaccinated with BCG.

As discussed above, Reed et al. merely teaches that where "more than one polypeptide is employed, the polypeptides used are preferably complementary . . . ." It does not teach that such combinations of polypeptides can be employed to distinguish between individuals that have been infected with tuberculosis and individuals that have been vaccinated with BCG. Moreover, Reed et al. does not even identify which sequences and polypeptides are encoded by BCG.

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Intern. Co. v. Teleflex*, 550 U.S. 398, 416 (2007). Appellant respectfully submits that the results yielded by the combinations of elements in the Pending Claims are not predictable in light of Reed et al. at least because (1) Reed et al. does not teach which sequences and polypeptides are encoded by BCG and (2) the particular combinations of the Pending Claims confer an additional function upon the

vectors, cells, and compositions created thereunder, e.g. the ability to distinguish between individuals that have been exposed to *M. tuberculosis* and individuals that have been vaccinated with BCG. Reed et al. does not teach combinations that possess such a function.

3. Reed et al. does not teach or fairly suggest the selection of a DNA sequence encoding MTBN4 for combination with additional elements to yield the vectors, cells, and compositions of the instant application.

Appellant submits that, in view of Reed et al., one of skill in the art would not have been motivated to create a vector, cell, or composition, comprising a DNA molecule or sequence encoding an MTBN4 polypeptide, wherein the polypeptide is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, as recited in the present claims. Appellant respectfully submits that one of skill in the art would not be motivated to: first (i) select the specific amino acid sequence described in Reed et al., i.e. SEQ ID NO:110, out of the extensive list of 209 possible sequence choices; and then (ii) incorporate a DNA sequence encoding that amino acid sequence into a vector, cell, or composition as presently claimed. In addition to the vast number of sequences listed in Reed et al., Appellant notes that SEQ ID NO:110 is mentioned only once in Reed et al. as a "partial sequence", with no description of its function, use, or characteristics.

Further, Appellant respectfully submits that, with respect to the first prong of the invention as set forth above wherein MTBN4 is selected, the selection of MTBN4 is analogous to a situation in which the prior art teaches a large genus that encompasses a claimed species. In both situations, (i) the prior art discloses a broad and generic class of components and (ii) the claimed invention somehow incorporates a single component from that class. "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to

establish a prima facie case of obviousness." MPEP 8th Edition, 7th revision, 2144.08 II citing *In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994). In *Baird*, the Court noted that while the prior art "unquestionably encompasse[d]" the claimed invention when certain variables were selected, there was nothing in the prior art suggesting that one should select the variables that would yield such an invention. *Baird* at 382. Appellant submits that the extensive set of 209 sequences contained in Reed et al. is analogous to the genus disclosed by the prior art in *Baird*. While Reed et al. discloses the amino acid sequence for SEQ ID NO:110, there is nothing in Reed et al. to suggest that one should select that particular amino acid sequence and combine a DNA molecule encoding that amino acid sequence with additional elements to yield the vectors, cells, and compositions claimed in the instant application. Therefore, just as the Court in *Baird* concluded that the prior art did not "teach or fairly suggest" the selection of variables that would yield the invention at issue in that case, Appellant respectfully submits that Reed et al. likewise does not teach or fairly suggest the selection of a DNA sequence encoding MTBN4 for combination with additional elements to yield the vectors, cells, and compositions of the instant application. Accordingly, Appellant respectfully submits that the Pending Claims are patentable under 35 USC §103(a) over Reed et al. at least because Reed et al. does not teach or fairly suggest the selection of a DNA sequence encoding MTBN4 for combination with additional elements to yield the vectors, cells, and compositions of the instant application. Additionally, for the reasons previously discussed herein, Appellant further submits that it would not have been obvious to one of skill in the art to then combine the DNA sequence encoding MTBN4 with the DNA sequence of another polypeptide that, like MTBN4, is (1) encoded by *M. tuberculosis* and (2) is not encoded by the BCG strain of *M. bovis*.

For the reasons stated above, Appellant believes that the Examiner's rejection of the Pending Claims under 35 USC §103(a) should be reversed and such action is respectfully requested.

CONCLUSION

For the reasons stated above, Appellant submits that the Pending Claims are patentable over Reed et al., and further submits that the rejections of the Pending Claims under 35 USC §103(a) are improper and should be withdrawn. Appellant respectfully request the Board to reverse the Examiner's rejections with instructions to allow the Pending Claims.

If any fees are deemed necessary for this Appeal Brief to be entered and considered, then the Commissioner is authorized to charge such fee to Deposit Account No. 50-1358. Appellant's undersigned attorney may be reached by telephone at (973) 422-6532 or by email at lschroeder@lowenstein.com. All correspondence should continue to be directed to the address below.

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VIII. CLAIMS APPENDIX

1-2. (Cancelled)

3. (Previously Presented) A vector comprising:

(a) a DNA sequence encoding a full length MTBN4 polypeptide, wherein the polypeptide is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*;

(b) at least one additional DNA sequence encoding a polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*; and

(c) each DNA sequence being operationally linked to a regulatory sequence allowing expression of the polypeptide encoded by each DNA sequence in a cell.

4. (Previously Presented) A vector comprising:

(a) a DNA sequence encoding a segment of a full length MTBN4 polypeptide, wherein said segment retains an antigenic property of the polypeptide and wherein the segment is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*;

(b) at least one additional DNA sequence encoding a segment of a full length polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*; and

(c) each DNA sequence being operationally linked to a regulatory sequence allowing expression of the segment encoded by each DNA sequence in a cell.

5. (Original) A cell transformed with the vector of claim 3.

6. (Original) A cell transformed with the vector of claim 4.

7. (Previously Presented) A composition comprising a vector and a pharmaceutically acceptable diluent or filler, wherein the vector comprises a DNA sequence encoding a full length MTBN4

polypeptide and wherein the polypeptide is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis* and at least one additional DNA sequence encoding a polypeptide which is encoded by *Mycobacterium tuberculosis* but is not encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*.

8. (Cancelled)

9. (Previously Presented) A composition comprising:

at least two DNA sequences, each encoding a polypeptide of the *Mycobacterium tuberculosis* complex that is not a polypeptide encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, and each being operationally linked to a regulatory sequence which allows expression of said polypeptide in a cell of a vertebrate, wherein at least one of said DNA sequences encodes a full length MTBN4 polypeptide.

10. (Previously Presented) A composition comprising:

at least two DNA sequences, each encoding a polypeptide of the *Mycobacterium tuberculosis* complex that is not a polypeptide encoded by the genome of the Bacille Calmette Guerin (BCG) strain of *Mycobacterium bovis*, and each being operationally linked to a regulatory sequence which allows expression of said polypeptide in a cell of a vertebrate, wherein at least one of said DNA sequences encodes a segment of a full length MTBN4 polypeptide, wherein said segment retains an antigenic property of the polypeptide.

11-54. (Cancelled)

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.